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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/068,725	02/06/2002	Wayne Kindsvogel	01-04	8714

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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	**PAPER NUMBER**
1643	

MAIL DATE	DELIVERY MODE
12/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/068,725	KINDSVOGEL, WAYNE	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10 and 25-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10 and 25-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 9 and 11-24 are canceled.

Claims 1 and 26-29 have been amended. Applicants' cooperation is requested in providing the correct status identifiers for the claims in future communications. e.g., see claims 28-29.

2. Claims 1-8, 10 and 25-32 are pending and under consideration.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Objections/Rejections Withdrawn

4. The objection to claims 26-27 in the recitation "wherein the binding to TACI within amino acids...", is withdrawn in view of the amendments to the claims.

5. The rejection of claims 1-3, 28 and 29 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation "antibody component" is withdrawn in view of the amendments to the claims.

Rejections Maintained

6. The rejection of claims 4-8, 10 and 25-27 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation "antibody component" is maintained.

The response filed 10/10/2007 states that the examiner is objecting to applicant being their own lexicographer, however, in the interest of compact prosecution, claims 1, 28 and 29 have been amended to recite "antibodies and fragments thereof". This has been fully considered but is not found persuasive. Claims 4-6, 8, 10 and 25 still recite an "antibody component" and as such claims 4-8, 10 and 25-27 remain rejected as set forth in the previous Office Action. The examiner agrees that applicant may act as his/her own lexicographer, however, this is not the basis of the instant rejection. Applicants' definition of an "antibody component" in the specification includes an entire antibody, antibody fragments, polyclonal antibodies, murine monoclonal antibodies,

humanized antibodies derived from murine monoclonal antibodies, chimeric antibodies, human monoclonal antibodies, and the like (see pg. 14, lines 30-31 and pg. 4, lines 27-29). It is unclear what "antibody component" is contemplated by "and the like", the specification does not define what is meant by "and the like", the terminology embraces antibody variants and fragments comprising amino acid substitutions, deletions, insertions, chemically derivatized antibodies, mimetics, a CDR, a framework, ect. There is no way for one skilled in the art to ascertain the requisite degree, direction or endpoint of an "antibody component" as defined by "and the like" and as such one of skill in the art would not be reasonably apprised of the metes and bounds of the claimed antibody components.

For these reasons and those already of record the rejection is maintained.

7. The rejection of claims 28-29 and 31-32 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as introducing new matter is maintained. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The response filed 10/10/2007 states that pg. 4, line 22 of the specification discloses anti-BCMA-TACI antibody components that bind a polypeptide having the amino acid sequence of amino acid residues 39 to 50 of SEQ ID NO:4 or a polypeptide having the amino acid sequence of amino acid residues 78 to 91 of SEQ ID NO:4. The examiner acknowledges the remainder of applicants' remarks, however, the present rejection does not question the support for an antibody that binds both BCMA and TACI, nor does it question support for binding to BCMA within amino acids 1 to 54 of SEQ ID NO:2 in view of the as filed specification at pg. 16, lines 24-27 as pointed to by applicant. Applicants' arguments with respect to the anti-BCMA-TACI antibody that binds within amino acids 39 to 50, or 78 to 91 of SEQ ID NO:4 have been fully considered but are not found persuasive. The as filed specification at pg. 4, lines 22-26

discloses that the anti-BCMA-TACI antibody components can bind a polypeptide having the amino acid sequence of amino acids 39 to 50 of SEQ ID NO:4 or a polypeptide having the amino acid sequence of amino acids 78 to 91 of SEQ ID NO:4. The transitional term "having" is interpreted as equivalent to "comprising" in light of the specification, where the transitional term "comprising" is inclusive or open-ended and does not exclude additional unrecited elements. See MPEP 2111.03. Thus, a polypeptide having the amino acid sequence of amino acids 39 to 50 of SEQ ID NO:4 or a polypeptide having the amino acid sequence of amino acids 78 to 91 of SEQ ID NO:4 is not limited to amino acids 39 to 50 of SEQ ID NO:4 or amino acids 78 to 91 of SEQ ID NO:4, but embraces SEQ ID NO:4, which is 293 amino acids in length. For example, SEQ ID NO:4 is merely one interpretation of "a polypeptide having the amino acid sequence of amino acids 39 to 50 of SEQ ID NO:4". As stated in the previous office Action, the specification does not provide any direction or guidance which would lead the skilled artisan to producing an anti-BCMA-TACI antibody wherein binding to TACI is within amino acids 39 to 50 of SEQ ID NO:4 or amino acids 78 to 91 of SEQ ID NO:4. The disclosure of an anti-BCMA-TACI antibody that binds a polypeptide having the amino acid sequence of amino acids 39 to 50 of SEQ ID NO:4 or a polypeptide having the amino acid sequence of amino acids 78 to 91 of SEQ ID NO:4 would not have led the skilled artisan to produce an anti-BCMA-TACI antibody that binds TACI within amino acids 39 to 50 or 78 to 91 of SEQ ID NO:4 as opposed to any other region within amino acids 1-293 of SEQ ID NO:4. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See *In re Smith* 173 USPQ 679, 683 (CCPA 1972).

Applicant is required to provide sufficient written support for the limitations recited in the claims in the specification or claims, as-filed, or remove these limitations from the claims in response to this Office Action.

For these reasons and those already of record the rejection is maintained.

8. The rejection of claims 1-8, 10 and 25-32 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inhibiting the proliferation of tumor cells comprising endogenous B-cell maturation antigen (BCMA) or transmembrane activator and calcium-modulator and cyclophilin ligand-interactor (TACI) comprising administering a composition comprising dual reactive BCMA-TACI monoclonal antibody, 255.7, (assuming the enablement of monoclonal antibody 255.7, i.e., biological deposit), or administering a composition comprising a bispecific BCMA-TACI antibody, wherein binding to BCMA is within amino acids 1 to 54 or 13 to 27 of SEQ ID NO:2 and the binding to TACI is within amino acids 30 to 67 or 68 to 154 of SEQ ID NO:4 and wherein the method further comprises the administration of an additional antibody that binds within amino acids 110 to 118 or 105 to 166 of SEQ ID NO:4, does not reasonably provide enablement for a method for inhibiting the proliferation of tumor cells comprising endogenous BCMA or TACI comprising administering a composition comprising an antibody component that binds BCMA and TACI, wherein binding to BCMA is within amino acids 1 to 54 or 13 to 27 of SEQ ID NO:2 and the binding to TACI is within amino acids 30 to 67 or 68 to 154 of SEQ ID NO:4, and wherein the method further comprises the administration of an additional antibody component that binds within amino acids 110 to 118 or 105 to 166 of SEQ ID NO:4 is maintained.

The response filed 10/10/2007 states that the claims recite an antibody or fragment thereof that binds both TACI and BCMA and any change to this defining structural characteristic would move the antibody (and thus the method of using that antibody) outside the scope of the claims. Applicant states that the specification also teaches a number of specific methods that can be used to determine whether the antibody does indeed bind both TACI and BCMA (pg. 17, lines 3-23). Applicant concludes that because of the specific structural characteristics that the antibodies must have in order to fall within the claims and the guidance provided by the specification to test for this characteristic, the present disclosure fully supports the recited methods of use of those antibodies. Applicants' arguments have been fully considered but are not found persuasive. While the claims require that the antibodies and fragments thereof

bind both BCMA and TACI thereby excluding those antibodies and fragments that do not bind both BCMA and TACI, the specification provides no guidance and direction to assist those skilled in the art in making and using the full scope of antibodies and fragments thereof that bind both BCMA and TACI. The art of Theill et al (U.S. Patent 6,774,106 B2; cited on PTO-892 mailed 7/20/06) teaches that there is significantly low homology between the cysteine rich extracellular regions of BCMA and TACI and in view of the evidence of Lederman et al (Molecular Immunology 28:1171-1181, 1991, of record) and Li et al (Proc. Natl. Acad. Sci. USA 77:3211-3214, 1980, of record), the skilled artisan could not predictably produce a monoclonal antibody or fragment thereof that binds to both BCMA and TACI. Although applicant discloses monoclonal antibody 255.7, which binds both BCMA and TACI, the dual specificity of monoclonal antibody 255.7 was an unexpected result in view of the low level of amino acid sequence identity shared by the extracellular domains of BCMA and TACI (Specification at pg. 3, lines 27-29). One of ordinary skill in the art could not predictably extrapolate the unexpected BCMA-TACI binding property of monoclonal antibody 255.7 to the genus of monoclonal antibodies (i.e., "antibody components") that bind both BCMA and TACI. It is unlikely that a monoclonal antibody produced against a polypeptide representing a fragment of the BCMA extracellular domain would also bind TACI, an unexpected property even for monoclonal antibody 255.7 according to applicant. Although, typically, inoperative embodiments are excluded by language in a claim (e.g., preamble), the scope of the claim may still not be enabled where undue experimentation is involved in determining those embodiments that are operable. Claims reading on significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative. *Atlas Powder Co. v. E.I. duPont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984); *In re Cook*, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971). One of skill in the art would neither expect nor predict the appropriate functioning of the antibodies as broadly as is claimed.

In view of the lack of the predictability of the art to which the invention pertains as evidenced by Lederman et al, Li et al and Theill et al the lack of guidance and direction

provided by applicant, and the absence of working examples, undue experimentation would be required to practice the claimed antibodies that bind both BCMA and TACI, commensurate in scope with the claimed invention. It is reiterated that the instant application is enabling for a method for inhibiting the proliferation of tumor cells comprising endogenous B-cell maturation antigen (BCMA) or transmembrane activator and calcium-modulator and cyclophilin ligand-interactor (TACI) comprising administering a composition comprising dual reactive BCMA-TACI monoclonal antibody, 255.7, (assuming the enablement of monoclonal antibody 255.7, i.e., biological deposit), or administering a composition comprising a bispecific BCMA-TACI antibody, wherein binding to BCMA is within amino acids 1 to 54 or 13 to 27 of SEQ ID NO:2 and the binding to TACI is within amino acids 30 to 67 or 68 to 154 of SEQ ID NO:4 and wherein the method further comprises the administration of an additional antibody that binds within amino acids 110 to 118 or 105 to 166 of SEQ ID NO:4.

9. The rejection of claims 1-8 and 26-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Theill et al (US Patent 6,774,106 B2, priority to 5/12/2000) in view of Gross et al (WO 00/40716, 7/13/2000) is maintained.

The response filed 10/10/2007 point out that the examiner has stated that "based on the low homology between the cysteine rich repeats of the extracellular domains of BCMA and TACI, it would not have been obvious to produce a monoclonal antibody that binds both BCMA and TACI within the claimed cysteine rich repeats of the extracellular domains (Office Action mailed 4/10/2007 at pg. 4, lines 8-12). Applicant states that because the presently claimed method utilizes an antibody that the examiner states is nonobvious, the method itself is also nonobvious. Applicant arguments have been fully considered but are not found persuasive. While the examiner has agreed with applicant that based on the low homology between the cysteine rich repeats of the extracellular domains of BCMA and TACI, it would have been nonobvious to produce a monoclonal antibody that binds both BCMA and TACI within the claimed cysteine rich repeats of the extracellular domains. However, it is noted that the feature upon which applicant relies

(i.e., monoclonal antibody that binds both BCMA and TACI) is not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Further, Theill teach that the antibody that binds both BCMA and TACI for inhibiting the proliferation of tumor cells can be a bispecific antibody or heteroantibody having two different antigen binding sites and Theill teach the cysteine rich repeats in the extracellular domains of both BCMA and TACI (see Figs. 11-12). Applicant has not provided any objective evidence that one of ordinary skill in the art would not have a reasonable expectation of success from the teachings in the prior art of obtaining a bispecific antibody that binds the cysteine rich repeat in the extracellular domains of both BCMA and TACI, particularly where the two antigen-binding sites are produced separately against the cysteine rich repeat of BCMA and the cysteine rich repeat of TACI.

Applicant states that the examiner has implied that since the low homology was presented as attorney argument, it somehow is less persuasive. Applicant is referring to the examiners' reply to applicants previous argument that the presently claimed antibodies are an unexpected result of screening antibodies that bound well to the TACI molecule for ability to bind BCMA in view that the cysteine rich repeats of the extracellular domains of BCMA and TACI share minimal homology, only on the order of 32.3% (see attached FASTA printout in the reply filed 1/19/2007). Again, the MPEP makes clear that allegations of unexpected results must be factually supported by an appropriate affidavit or declaration to be of probative value (see MPEP 716.01(c)).

As discussed supra, the instant rejection is being maintained based on the finding that one of ordinary skill in the art would have been motivated and had a reasonable expectation of success to produce a method of inhibiting tumor cell proliferation comprising administering a bispecific antibody that binds the cysteine rich repeat in the extracellular domains of both BCMA and TACI and the BCMA-TACI antibody is conjugated to a therapeutic or diagnostic agent fro therapeutic benefit in lymphoma patients in view of Theill et al and Gross et al.

Therefore, for these reasons and those already of record, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references and the rejection is maintained.

10. No claim is allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643